



mSphere of Influence: Drivers of Host-Associated Microbial Community Structure and Change

 Vanessa L. Hale^a

^aVeterinary Preventive Medicine, Ohio State University College of Veterinary Medicine, Columbus, Ohio, USA

ABSTRACT Vanessa L. Hale studies the role of the microbiome in disease susceptibility in animal and human health. In this mSphere of Influence article, she reflects on how the papers “Evolution of mammals and their gut microbes” (R. E. Ley, M. Hamady, C. Lozupone, P. J. Turnbaugh, et al., *Science* 320:1647–1651, 2008, <https://doi.org/10.1126/science.1155725>) and “A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility” (M. S. Desai, A. M. Seekatz, N. M. Koropatkin, N. Kamada, et al., *Cell* 167:1339–1353.e21, 2016, <https://doi.org/10.1016/j.cell.2016.10.043>) have provided a foundation for studying drivers of gut microbial structure and change across host species in the context of evolution and disease risk.

KEYWORDS diet, evolution, fiber, gut microbiome, gut microbiota


What are the ultimate and proximate drivers of host-associated microbial community structure and change? Work across disciplines from medicine to agriculture to anthropology actively seeks to answer this question in part by determining how these communities can be manipulated to promote health and prevent or treat disease. Two papers that set the stage for current work and profoundly shaped my own thinking include Ley et al. (2008), “Evolution of mammals and their gut microbes,” and Desai et al. (2016), “A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility” (1, 2). Ley’s paper (from J. I. Gordon’s research group) framed gut microbial communities on a long-term evolutionary time scale and demonstrated that host diet (herbivore, omnivore, carnivore) and phylogeny shape gut microbial diversity between hosts. Desai’s work (from E. C. Martens’ research group) illustrated microbial community change within hosts on a short-term, daily time scale and how diet-microbe interactions impact host health and enteric pathogen susceptibility. Both studies examine factors that shape gut microbial communities but on two very different time scales.

Ley et al. (2008) compared the gut microbial communities of 60 animal species, including humans, and evaluated the influence of diet, host taxonomic order, and sample provenance on gut microbial composition and diversity across host species. The authors hypothesized that gut microbiota play a critical role in the acquisition of new dietary niches, which can ultimately lead to speciation. They identified similarities in microbial communities based on host diet and phylogeny, and they made several unexpected observations: foregut and hindgut fermenting herbivores had similar diets but distinct microbial communities; herbivorous pandas, with simple guts, had microbial communities similar to other simple-gutted carnivores despite their dietary differences; and humans had microbial communities similar to other omnivorous species. This work provided a foundation for future studies on the gut microbiome and evolution/coevolution, diet, fiber consumption, and host physiology (3, 4), and it paved a way for thinking about translational models for microbiome research. Desai et al. (2016) evaluated many of the same factors—diet, fiber consumption, host physiology—in

Citation Hale VL. 2021. mSphere of Influence: drivers of host-associated microbial community structure and change. *mSphere* 6: e00248-21. <https://doi.org/10.1128/mSphere.00248-21>.

Copyright © 2021 Hale. This is an open-access article distributed under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/).

Address correspondence to Vanessa L. Hale, hale.502@osu.edu.

 @Hale_Microbes reflects on 2 key papers that shaped her thinking about drivers of gut microbial community change: Ley et al. 2008, <https://science.sciencemag.org/content/320/5883/1647>; Desai et al. 2016, <http://dx.doi.org/10.1016/j.cell.2016.10.043>

The views expressed in this article do not necessarily reflect the views of the journal or of ASM.

Published 7 April 2021

a series of experiments that examined gut microbial community function and change over time in response to differing dietary regimens. In their germfree mouse model inoculated with a synthetic human gut microbiota, fiber-free diets or alternating fiber-rich/fiber-free diets resulted in an increased abundance of mucin-degrading bacteria, an increase in microbial mucus-targeting transcripts, a thinner mucus layer in the mouse gut, a decreased colon length, and an increase in gut inflammatory markers. These changes increased susceptibility to the enteric pathogen *Citrobacter rodentium*, which is a mouse model for enteropathogenic *Escherichia coli*. This work is an elegant example, among others (5, 6), revealing that “one microbe” does not automatically equal “one disease”; rather, there is a rich interaction between microbial communities, diet, and host mucin production, which affects disease susceptibility and pathogenesis.

The question at the core of my research is: how do host-associated microbial communities shape disease susceptibility in animals? I study animal models of diseases including clostridial enteritis and bladder cancer that have translational relevance to human health. From a 30,000-foot view, this requires me to consider how similarities or differences in host taxa broadly impact microbial community structure, host-microbe relationships, and disease risks between species. At a finer scale, I evaluate how microbes interact within communities and hosts, and in response to external factors like diet or xenobiotics. Both the Ley and Desai papers expanded my scientific horizons by revealing how we could study microbial communities from ultimate and proximate perspectives. The Ley et al. paper applied recently developed tools (UniFrac) for comparing microbial communities (7, 8), while the Desai et al. paper applied a tour de force of both established and novel methodologies for studying the microbiota—ranging from culture and histopathology, to gnotobiotic mouse models, to designing a synthetic microbial community, to laser capture microdissection of a colon section for separate analyses of lumen and mucus layers, to transcriptomics and metabolomics, to alcian blue and MUC2 staining for measuring mucin thickness. At different levels, both of these papers captured my scientific imagination and showed me how I could work at the intersection of animal and human health studying the effects of microbial communities on disease susceptibility.

REFERENCES

1. Ley RE, Hamady M, Lozupone C, Turnbaugh PJ, Ramey RR, Bircher JS, Schlegel ML, Tucker TA, Schrenzel MD, Knight R, Gordon JL. 2008. Evolution of mammals and their gut microbes. *Science* 320:1647–1651. <https://doi.org/10.1126/science.1155725>.
2. Desai MS, Seekatz AM, Koropatkin NM, Kamada N, Hickey CA, Wolter M, Pudlo NA, Kitamoto S, Terrapon N, Muller A, Young VB, Henrissat B, Wilmes P, Stappenbeck TS, Núñez G, Martens EC. 2016. A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility. *Cell* 167:1339–1353.e21. <https://doi.org/10.1016/j.cell.2016.10.043>.
3. Amato KR, Sanders J, Song SJ, Nute M, Metcalf JL, Thompson LR, Morton JT, Amir A, McKenzie V, Humphrey G, Gogul G, Gaffney J, Baden A, Britton G AO, Cuzzo P, Di Fiore A, Dominy J, Goldberg L, Gomez A, Kowalewski MM, Lewis R, Link A, Sauter M, Tecot S, White B, Nelson K, Stumpf R, Knight R, Leigh S. 2019. Evolutionary trends in host physiology outweigh dietary niche in structuring primate gut microbiomes. *ISME J* 13:576–587. <https://doi.org/10.1038/s41396-018-0175-0>.
4. Clayton JB, Vangay P, Huang H, Ward T, Hillmann BM, Al-Ghalith GA, Travis DA, Long HT, Tuan BV, Minh VV, Cabana F, Nadler T, Toddes B, Murphy T, Glander KE, Johnson TJ, Knights D. 2016. Captivity humanizes the primate microbiome. *Proc Natl Acad Sci U S A* 113:10376–10381. <https://doi.org/10.1073/pnas.1521835113>.
5. Buffie CG, Bucci V, Stein RR, McKenney PT, Ling L, Gobourne A, No D, Liu H, Kinnebrew M, Viale A, Littmann E, van den Brink MRM, Jenq RR, Taur Y, Sander C, Cross JR, Toussaint NC, Xavier JB, Pamer EG. 2015. Precision microbiome reconstitution restores bile acid mediated resistance to *Clostridium difficile*. *Nature* 517:205–208. <https://doi.org/10.1038/nature13828>.
6. Hryckowian AJ, Van Treuren W, Smits SA, Davis NM, Gardner JO, Bouley DM, Sonnenburg JL. 2018. Microbiota-accessible carbohydrates suppress *Clostridium difficile* infection in a murine model. *Nat Microbiol* 3:662–669. <https://doi.org/10.1038/s41564-018-0150-6>.
7. Lozupone C, Knight R. 2005. UniFrac: a new phylogenetic method for comparing microbial communities. *Appl Environ Microbiol* 71:8228–8235. <https://doi.org/10.1128/AEM.71.12.8228-8235.2005>.
8. Lozupone CA, Hamady M, Kelley ST, Knight R. 2007. Quantitative and qualitative β diversity measures lead to different insights into factors that structure microbial communities. *Appl Environ Microbiol* 73:1576–1585. <https://doi.org/10.1128/AEM.01996-06>.